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EXAMINER	
GAMBEL, P	

ART UNIT	PAPER NUMBER
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SETH A. FIDEL PH. D.
ALEXION PHARMACERTICALS, INC.
25 SCIENCE PARK - SUITE 360
NEW HAVEN, CT 06511

DATE MAILED: 05/22/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☑ Responsive to communication filed on 3/15/96 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☑ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☑ Claims 1-5 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☑ Claims 6-9 have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☑ Claims 1-5 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.

13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

15. The Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1816.

16. According to applicant's amendment, filed 3/15/96 (Paper No. 9), claims 6-9 have been canceled and claim 1 has been amended.

Claims 1-5 are pending and under consideration.

REJECTIONS WHICH STILL REMAIN AND RESPONSE TO APPLICANT'S ARGUMENTS

17. Formal photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the form PTO-948 previously sent in Paper No. 6.

Photographs are not acceptable until petition is granted as set forth in 37 CFR 1.84(b). Under 37 CFR 1.84(b), the applicant must file a petition with fee requesting acceptance of the black and white photographs. The petition is decided in the Office of the Group Director.

18. The previous objection/rejection of the instant claimed methods drawn to inhibiting glomerulonephritis with C%-specific antibodies under 35 U.S.C. § 112, first paragraph, has been withdrawn upon reconsideration of Examples 1-3 of the instant application, an updated search and applicant's arguments in conjunction with Matis, Rollins and Alford declarations, filed 4/16/94, under 37 C.F.R. § 1.132.

19. The previous rejections of claim 1-8 under 35 U.S.C. § 112, second paragraph, have been withdrawn in response to applicant's amended and cancelled claims.

20. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. , Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

21. Claims 1-5 are rejected under 35 U.S.C. § 103 as being unpatentable over Wurzner et al. (Complement Inflamm., 1991; # 20) in view Couser et al. (J. Am. Soc. Nephrol., 1991; 1449, #5) and Sims et al. (U.S. Patent No. 5,135,916; 1449, #1). Claims 1-5 are drawn to the use of C5/C5b-specific antibodies to inhibit complement in the treatment of glomerulonephritis.

Wurzner et al. teach the claimed C5-specific antibodies, as disclosed in example 1 of the specification (see entire document). These C5-specific antibodies exhibited strong inhibitory activities with respect to terminal complement complex generation, C5a generation and complement-mediated hemolysis (see Results, particularly pages 334-335). It is noted that the anti-C5-specific antibodies exhibited stronger inhibitory activity than C6-specific antibodies in hemolysis assays (see page 336, column 2). Wurzner et al. clearly teaches the application of C5 (and C6) depletion in various diseases including glomerulonephritis and nephritis (Discussion, particularly, page 337). Wurzner et al. concludes that the biological consequences of C5a and terminal complement complex generation can be circumvented by these monoclonal antibodies (see Discussion). The instant antibodies taught by Wurzner et al. were employed in a number of immunological assays, which would have required the use of standard buffers (see Materials and Methods) and their storage. Such buffers as PBS were well known in the art for the storage and use of antibodies. Also, the reference teaches the use of these antibodies in analyzing the specific regions on C5 and C6 which are involved in complement complex formation (see Discussion, final paragraph).

Couser et al. references teach the role of complement including the role of C5b-9 in mediating glomerulonephritis (see entire document). Couser et al. (JASN, 1991) teach that C6 depletion studies including the use of antibodies to deplete C6 could ameliorate the deleterious effects of complement deposition and activation (Introduction). In the Discussion, it is taught that the mechanism of action by which C6 works is through C5b-9 (page 898, for example).

It was art-known at the time the invention was made that C5b-9 is a complex that results from proteolytic cleavage of C5 to generate C5b which then combines with C6 and C7 to form Cb5,6,7.

As a general teaching reference, Sims et al. teach making C5b-9 specific inhibitors antibodies for inhibiting complement activation associated with autoimmune disorders (see entire document including Summary of the Invention and column 3, lines 20-23. This reference teaches the storage and in vitro and in vivo use of C5b-9 inhibitors.

Therefore, the ordinary artisan was motivated at the time the invention was made to make C5b-9 inhibitors as a means to treat complement-mediated pathology associated with glomerulonephritis, as taught by the references above. Wurzner et al. teach that the instant antibodies had features such as inhibitory activities with respect to terminal complement complex generation, C5a generation and complement-mediated hemolysis, that were particularly attractive as therapeutic agents to block complement-mediated effects in vivo. In addition, Wurzner et al. teach that these features of the instant antibodies had advantages over C6-specific antibodies that also operate as C5b-9 inhibitors, as taught by Wurzner et al. and Crouser et al. Since C6-specific antibodies exemplify in vivo inhibitory effects as taught by Couser; the ordinary artisan would have had motivation to apply the instant C5-specific antibodies in the same or similar treatment methods of ameliorating nephritis.

Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to apply C5/C5b-specific antibodies as complement inhibitors in the treatment of glomerulonephritis. From the teachings of the reference, it was apparent one of ordinary skill in the would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention was a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

22. Applicant's arguments, filed 3/15/96 (Paper No. 9) and 4/16/96 (Paper No. 10) in conjunction with the with Matis and Rollins declarations, filed 4/16/94 (Paper No. 10), under 37 C.F.R. § 1.132 have been fully considered but are not found convincing.

Applicant in conjunction with Matis and Rollins argue that it would be counterintuitive to treat a disease with antibodies that could result in more antigen-antibody complexes; that the monoclonal antibodies of the instant invention would not meet the criteria set forth by Kalli (Springer Semin. Immunopathol, 1994; 892 of record); that the prior art would not have indicated that complement inactivation alone would be effective; that there were no expectation of success and that there was a long felt need.

In contrast, the prior art of record clearly teaches the contribution of complement to glomerulonephritis and the inhibition of glomerulonephritis with the complement-specific antibodies of the instant invention. As set forth above, Wurzner et al. teach clearly teaches that the biological consequences of C5a and terminal complement complex generation can be circumvented by the instant C5-specific monoclonal antibodies having appropriate strong inhibitory activities (see entire document, particularly the Discussion). Applicant's arguments have not addressed the prior art of record in the rejection under 35 U.S.C. § 103, particularly Wurzner et al.; where there is clear teaching and direction of applying the instant methods in treating glomerulonephritis with an expectation of success. The combined teachings of record clearly teach inhibiting complement including C5/C5b would be beneficial in treating glomerulonephritis. In contrast, applicant has addressed the prior art in a more generic manner or with references presented in the previous rejection under 35 U.S.C. § 112, first paragraph. The combined teachings particularly Wurzner et al. provide clear direction, motivation and expectation of success in treating glomerulonephritis with C5/C5b-specific antibodies. Applicant's arguments including the issue of long-felt need are not found persuasive of patentability when the claimed invention would flow logically from the teaching of the prior art of record.

23. The previous rejection of claims 6-9 under 35 U.S.C. § 103 as being unpatentable over Wurzner et al. (Complement Inflamm., 1991; 1449, #20) has been withdrawn in view of the cancellation of these claims.

24. No claim is allowed.

25. Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

26. This application is subject to the provisions of Public Law 103-465, effective June 8, 1995. Accordingly, since this application has been pending for at least two years as of June 8, 1995, taking into account any reference to an earlier filed application under 35 U.S.C. 120, 121 or 365(c), applicant, under 37 CFR 1.129(a), is entitled to have a first submission entered and considered on the merits if, prior to abandonment, the submission and the fee set forth in 37 CFR 1.17(r) are filed prior to the filing of an appeal brief under 37 CFR 1.192. Upon the timely filing of a first submission and the appropriate fee of $375 for a small entity under 37 CFR 1.17(r), the finality of the previous Office action will be withdrawn. In view of 35 U.S.C. 132, no amendment considered as a result of payment of the fee set forth in 37 CFR 1.17(r) may introduce new matter into the disclosure of the application.

If applicant has filed multiple proposed amendments which, when entered, would conflict with one another, specific instructions for entry or non-entry of each such amendment should be provided upon payment of any fee under 37 CFR 1.17(r).

27. Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242 or (703) 305-7939.

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1800 receptionist whose telephone number is (703) 308-0196.

Phillip Gambel, Ph.D.
Patent Examiner
Group 1800
May 15, 1996

CHRISTINA Y. CHAN
SUPERVISORY PATENT EXAMINER
GROUP 1800